Journal of the American College of Cardiology
© 2011 by the American College of Cardiology Foundation
Published by Elsevier Inc.
Vol. 58, No. 9, 2011
ISSN 0735-1097/$36.00
doi:10.1016/j.jacc.2011.04.029

Valvular Aortic Stenosis as a Major Sequelae in Patients With Pre-Existing Subaortic Stenosis

Changing Spectrum of Outcomes

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Objectives The purpose of this study was to determine the prevalence of valvular aortic stenosis requiring surgery in patients with a pre-existing diagnosis of subaortic stenosis.

Background Classic teachings emphasize aortic regurgitation as the most common complication associated with discrete subaortic stenosis. We hypothesized that significant aortic stenosis may also be an important valve lesion associated with this condition.

Methods Clinical outcomes in patients with subaortic stenosis were examined. The primary outcome of interest was the prevalence of valvular aortic stenosis requiring surgery (surgical valvotomy or valve replacement). Logistic regression was used to identify variables associated with the need for surgery for aortic stenosis.

Results One hundred twenty-one adults with subaortic stenosis (median age 32 years) were evaluated in our clinic. Associated lesions were common: 23% had bicuspid valves and 21% had coarctation of the aorta. Seventy-nine percent of the patients had at least 1 surgical resection of subaortic tissue (median age 12 years). Moderate to severe aortic regurgitation was present in 16% of patients (19 of 121), 3 of whom required surgical intervention in adulthood. Twenty-six percent of patients (32 of 121) required surgery for valvular aortic stenosis. Valve surgery for aortic stenosis was more common in patients with concomitant bicuspid aortic valve disease ($p = 0.008$), coarctation of the aorta ($p = 0.03$), and supravalvular stenosis ($p = 0.02$).

Conclusions Valvular aortic stenosis is a surprisingly common finding in patients with discrete subaortic stenosis. Careful clinical follow-up of this population to monitor aortic valve status continues to be warranted even after a successful surgical resection. (J Am Coll Cardiol 2011;58:962–5) © 2011 by the American College of Cardiology Foundation

Subaortic stenosis is an important condition, accounting for approximately 8% to 20% of all congenital left ventricular outflow tract (LVOT) obstructions (1,2). Subaortic stenosis is notable for its variable, but sometimes rapid progression and high rates of recurrence after surgical repair (1–4). The most commonly described hemodynamic sequelae in patients with subaortic stenosis is aortic regurgitation, which has been estimated to occur to some degree in 30% to 50% of pediatric patients and as many as 80% of adult patients (2,3,5). Damage to the aortic valve and subsequent regurgitation is thought to be secondary to the subvalvular high-velocity systolic jet produced by the outflow tract obstruction (2,3,5–9). The current surgical approach favors early resection of the subaortic tissue in an attempt to prevent the acquired damage to the aortic valve (1,3,6,8,10–12).

Although the prevalence of aortic regurgitation has been well described in this population, little information is available regarding the prevalence of aortic stenosis in the pediatric or adult population. We hypothesized that with early surgical resection of the subaortic tissue, longer follow-up will identify aortic stenosis as an important valve lesion associated with this condition. Thus, the objectives of this study were to determine the prevalence of significant valvular aortic stenosis in adults with subaortic stenosis and to identify determinants of valvular aortic stenosis requiring surgery.

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Manuscript received January 24, 2011; revised manuscript received April 21, 2011, accepted April 27, 2011.

Methods

All adult patients (age older than 17 years) with a pre-existing diagnosis of congenital discrete fibromuscular subaortic stenosis seen at the Toronto Congenital Cardiac Centre for Adults (Toronto, Ontario, Canada) were included in the study. Patients with the following associated anomalies were excluded: atrioventricular septal defects, ventricular septal defects, transposition of the great arteries, double outlet right ventricle, hypertrophic cardiomyopathy, and univentricular connections.

Clinical and surgical information was obtained from chart abstraction. Surgical notes were unavailable for 3 patients who had interventions outside the country. Echocardiographic data were obtained from the last available echocardiogram before surgical intervention for patients who had undergone surgery for aortic stenosis (≤1 year before intervention) or at the most recent clinical follow-up visit for others. Peak LVOT gradients were calculated using the modified Bernoulli equation (13). The degree of aortic regurgitation was assessed by experienced echocardiographers and graded as mild, moderate, or severe using Doppler criteria (14). Bicuspid aortic valve anatomy was confirmed echocardiographically or at the time of surgery.

The primary endpoint included any aortic valve surgery (surgical valvotomy or aortic valve replacement) for significant aortic stenosis. Although all patients followed at the Toronto Congenital Cardiac Centre for Adults were at least 17 years of age, many had undergone aortic valve intervention for aortic stenosis in childhood (n = 15). All operative reports were verified by the primary investigator.

Statistical analysis. Data analysis was performed using SPSS version 10.0 (SPSS, Inc., Chicago, Illinois). Logistic regression was used to determine clinical and echocardiographic variables associated with aortic stenosis requiring surgery. The level of statistical significance was set at 0.05 (2-sided).

Results

One hundred twenty-one patients met inclusion criteria. Fifty-six percent of patients had additional congenital lesions including bicuspid aortic valve, coarctation of the aorta, and supravalvular aortic stenosis (Table 1).

The median age of the cohort at the end of follow-up or at the time of surgery for aortic stenosis was 32 years (range 1 to 81 years). Significant valvular aortic stenosis requiring surgery was present in 26% (32 of 121) of patients. Three patients had mixed aortic valve disease with at least moderate aortic regurgitation; however, their main indication for surgery was aortic stenosis. The mean age at surgical intervention was 16 years (range 1 to 51 years). The types of surgical interventions are presented in Table 2.

Both bicuspid aortic valve disease and coarctation of the aorta were present in 8 patients who required aortic valve surgery for aortic stenosis. However, the majority (60%, 19 of 32) of patients requiring valve surgery for aortic stenosis did not have bicuspid valves.

Moderate to severe aortic regurgitation was present in 16% (19 of 121) of patients at last follow-up or before surgery. Of the 19 patients with significant aortic regurgitation, only 3 required aortic valve surgery for aortic regurgitation, all of which occurred in adulthood. None of the patients requiring aortic valve surgery for aortic regurgitation had concomitant aortic stenosis.

For comparison, the study cohort was divided into 2 groups: patients who required aortic valve surgery for aortic stenosis (n = 32) and patients who did not undergo valve surgery for aortic stenosis (n = 89) (Table 3). The median age of patients requiring valve surgery for aortic stenosis at the time of surgical intervention was 16 years (range 1 to 51 years). For patients not undergoing surgery for aortic stenosis, the median age at the time of last available follow-up visit was 30 years (range 18 to 73 years). There was a higher prevalence of bicuspid aortic valves ($p = 0.008$), coarctation of the aorta ($p = 0.03$), and supravalvular aortic stenosis ($p = 0.02$) in the group of patients requiring surgery for aortic stenosis. There was a trend toward intervention for aortic stenosis in patients who required a reoperation for recurrent subaortic stenosis ($p = 0.08$).

Abbreviations and Acronyms

LVOT = left ventricular outflow tract

Discussion

This is the first study to focus on the high prevalence of stenotic aortic valve disease in patients with pre-existing fibromuscular subaortic stenosis. Aortic stenosis is an out-

Table 1 Baseline Characteristics

Male	65 (54)
Associated anomalies	68 (56)
Bicuspid aortic valve*	28 (23)
Coarctation of the aorta*	25 (21)
Supravalvular aortic stenosis*	12 (10)
Surgical resection of subaortic tissue†	95 (79)
Surgery for recurring subaortic stenosis	28
Patients never requiring resection of subaortic tissue	26 (21)
Age at first resection, yrs	12 (1–67)
Peak LVOT gradient at first resection (n = 72), mm Hg	72 ± 28
Other surgeries performed during follow-up†	
Coarctation repair	20
Konno procedure	5
Patent ductus arteriosus ligation	4
Supravalvular aortic repair	3
Mitral valvotomy	2
Ross procedure	2
Atrial septal defect closure	1

n = 121. Values are n, n (%), median (range), or mean ± SD. *Diagnoses are not mutually exclusive. †Surgeries are not mutually exclusive.
LVOT = left ventricular outflow tract.

Table 2 Surgical Outcomes

Any surgery for aortic stenosis	32 (26)
Aortic valve replacement	9
Surgical valvotomy	23
Reoperation for valve replacement post-valvotomy	12/23
Age at surgery for aortic stenosis, yrs	
Median and range	16 (1–51)
Surgery for aortic stenosis in adulthood (age >17 yrs)	15

n = 121. Values are n (%), n, or n/N.

come often underappreciated in this population. We found that surgery for aortic stenosis was more common than surgery for aortic regurgitation. Concomitant bicuspid aortic valves, coarctation of the aorta, and supravalvular stenosis were associated with an increased risk of surgery for aortic stenosis.

Our population is similar to those described in other studies with respect to prevalence of associated congenital heart defects (2–5,10,15) prevalence of bicuspid aortic valves (4,8,16), the severity of subaortic disease (6,8), and the frequency of some degree of aortic regurgitation (2,3). However, this study differed from previously published studies that consisted primarily of pediatric patients with shorter follow-up (1–3,17). In our study, longer follow-up after early resection has demonstrated an altered natural history with less subsequent aortic regurgitation and more significant stenotic lesions.

The most comparable series is that by Oliver et al. (5) that described 134 adults with discrete subaortic stenosis. Similar to our findings, they demonstrated that <20% of patients had hemodynamically significant aortic insufficiency and that there was progression of the LVOT obstruction over time. However, they did not report on the prevalence of valvotomy and valve replacement. In addition, our study population more commonly required surgical resection of subaortic tissue and included more patients with associated bicuspid aortic valves and supravalvular aortic stenosis, factors that may contribute to a higher risk of the development of aortic stenosis in late follow-up.

There are a number of other reasons that aortic stenosis may develop in patients after subaortic resection. Despite resection of subvalvular tissue, the valve may still be exposed to abnormal fluid dynamic forces related to high preoperative gradients or be affected by recurrent subaortic stenosis, or there may be an intrinsically abnormal LVOT architecture. Aortic thickening on direct surgical inspection, thought to be secondary to high preoperative subvalvular gradients, has been previously reported in a pediatric cohort of patients who underwent early surgical resection (32% of patients), and the length of follow-up was the only independent risk factor identified (6). In our study, there was a trend toward intervention for aortic stenosis in patients who required a reoperation for recurrent subaortic stenosis. Patients with subaortic stenosis have been reported to have a longer and narrower LVOT, which may also contribute to the proliferation of the stenotic lesions in response to the turbulent flow and the high shear stress produced (15).

Patients with bicuspid aortic valves are at risk of age-dependent progression of aortic valve disease (18). Michelena et al. (19) found that 12% of asymptomatic patients with a diagnosis of bicuspid aortic valves required aortic valve repair for aortic stenosis (mean age at surgery, 49 ± 20 years). Although this may contribute in part to our findings, in our series, the majority of patients (60%) requiring valve surgery were not identified as having a congenitally abnormal valve. Furthermore, the mean age at surgical intervention was only 19 ± 14 years; much younger than in the bicuspid valve series. These observations suggest that factors other than the congenitally abnormal bicuspid valves play a role in the development of aortic stenosis.

Supravalvular aortic stenosis and coarctation were associated with aortic stenosis requiring intervention. This finding raises the possibility that the hemodynamics of high-velocity blood flow above the valve may influences outcomes at the valvular level.

Study limitations. This study was a retrospective study of patients followed in an adult congenital clinic, and therefore a survival bias and/or a referral bias may exist. Measures of the true prevalence of disease need to be corroborated with

Table 3 Determinants of Interventions for Aortic Stenosis in Patients With Discrete Subaortic Stenosis

	Aortic Stenosis Requiring Surgery (n = 32)	No Aortic Stenosis Requiring Surgery (n = 89)	Odds Ratio (95% CI)	p Value
Associated cardiac lesions				
Bicuspid aortic valve	13 (41)	15 (17)	3.4 (1.4–8.3)	0.008
Coarctation of the aorta	11 (34)	14 (16)	2.8 (1.1–7.1)	0.03
Supravalvular aortic stenosis	8 (25)	4 (4)	4.9 (1.3–18.7)	0.02
Surgical history				
Median age at first resection, yrs	15	14	1.0 (0.97–1.0)	0.87
Resection before the age 18 yrs	21 (66)	47 (53)	1.7 (0.7–4.0)	0.20
LVOT peak gradient pre-operatively before first subaortic resection, mm Hg	80 ± 30 (n =23)	67 ± 27 (n = 47)	1.0 (1.0–1.0)	0.53
Reoperation for recurrent subaortic stenosis at or before endpoint	11 (34)	17 (19)	2.2 (0.9–5.5)	0.08

Values are n (%), n, or mean ± SD.
CI = confidence interval; LVOT = left ventricular outflow tract.

further studies that capture the pediatric population from birth. Echocardiographic data were unavailable for some early pediatric patients undergoing resection because this imaging modality was not yet routinely used. Because aortic annular dimensions were not consistently available, we cannot comment on the impact of annular hypoplasia on outcomes.

Conclusions

The limited occurrence of severe aortic regurgitation in the long-term follow-up of adult patients with subaortic resection seems to suggest that surgical resection of significant subaortic obstructions has provided some protection against aortic regurgitation. In this cohort, surgical interventions for aortic stenosis occurred more frequently than interventions for aortic regurgitation. Bicuspid aortic valve disease, coarctation of the aorta, and supravalvular aortic stenosis were associated with the need for aortic stenosis surgery. Careful clinical follow-up of this adult population to monitor aortic valve status continues to be warranted even after a successful surgical resection.

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Key Words: aortic valve disease ▪ congenital heart defects ▪ subaortic stenosis.